

HCV ADVOCATE WEEKLY NEWS REVIEW

Review of HCV, HBV and HIV/HCV Coinfection Related News and Highlights

*Alan Franciscus
Editor-in-Chief*

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May 30, 2009

FDA faults hospital's handling of donor blood

<http://www.southbendtribune.com>

Jeff Parrott

Tribune Staff Writer

Elkhart General warned after 2 patients got blood from donor with hepatitis C.

Elkhart General Hospital, after learning that a donor's blood tested positive for antibodies to the hepatitis C virus, violated federal regulations by later accepting the person's subsequent blood donations and giving it to two patients, according to federal inspectors.

Because antibodies are what the body creates to fight off a particular disease, their presence indicates that the donor had been infected with the virus, either in the past or at the time the donations were made. In these cases, "confirmatory" testing for the virus itself was "indeterminate," meaning it was not clearly negative or positive, officials with the U.S. Food and Drug Administration told *The Tribune*.

Donors who test positive for hepatitis C antibodies must be permanently banned from donating, according to the hospital's standard operating procedures, which are patterned after federal regulations, FDA Detroit District Office Director Joann M. Givens said in a "warning letter" sent earlier this month to Elkhart General President Gregory Lintjer.

The Tribune received a copy of the letter from a man who said he works in Elkhart.

The FDA knew of no one who received the blood becoming infected, agency spokeswoman Susan Cruzan said.

Gregory Losasso, the hospital's vice president of operations, told *The Tribune* that no one received infected blood. He said the donor in question tested positive for the hepatitis C antibodies in November 2007, then came back and donated on April 29, 2008, and again on Aug. 30, 2008.

Losasso said it turned out that the first test yielded a "false positive," or the donor no longer had the virus, and the blood was deemed safe for the two transfusions given to other patients.

"No contaminated units of blood were used, nor was there a risk of them ever being used on patients," Losasso said. "The FDA would likely have closed us down. That's how serious it would have been."

He said the hospital's only mistake was allowing the donor to donate again five months after he tested positive in November. Federal regulations require a blood bank to wait six months, he said.

Losasso said all blood donated to the hospital is tested by the South Bend Medical Foundation before it is transfused into recipient patients.

The violation was one of several found in a routine FDA inspection of the hospital's Blood Donor Center from Dec. 1 through Dec. 10.

Inspectors also determined:

- After two patients' blood tested positive for antibodies to the AIDS virus, types 1 and 2, the center failed to add their names to a list of "unsuitable donors," so that their blood could never be distributed for transfusions to other patients in the future. These two people had donated blood to be transfused back into their own bodies later, as happens in non-emergency surgeries.
- The center failed to record as unsuitable a person whose blood tested positive on three occasions for hepatitis B antibodies. This person also had been donating blood for his or her own future use.
- After a donor's blood tested positive for syphilis, the center failed to add him or her to the unsuitable list.
- Under the center's standard operating procedures, a donor who more than once tests positive for hepatitis B but who tests negative once on a confirmatory test, which is more specific, is not banned from future donations. But federal regulations require them to be.
- The center's standard operating procedures did not include a written description of its procedures for coding and labeling of blood containers, which must include safeguards to

avoid labeling mix-ups.

- The center had no written description of its policy on notifying donors with "abnormal test results."

According to the warning letter, dated May 6, the FDA was satisfied with corrective actions the hospital took in February in response to the inspection findings. However, the FDA said it remained concerned that the center's procedures on denying donors' blood because it is tainted, along with "lookback investigations," are not in step with current federal regulations.

Lookback is the identification of recipients of potentially contaminated blood.

Losasso declined to comment in detail on the inspection's findings.

"Most of it is documentation, and we have corrected those things," he said. "We had a fairly manual process. We've converted a lot to computers, and we had a transition in management during that time."

Red Cross, hospital sued over 'botched' blood transfusion

<http://www.canberratimes.com.au>

Noel Towell

A young Canberra man is suing the Red Cross Blood Service and the Calvary Hospital over an alleged botched blood transfusion 25 years ago that left him battling with a chronic illness.

Papers lodged with the ACT Supreme Court allege that the man was given two blood transfusions at the Belconnen hospital soon after he was born there on February 11, 1984.

He says the transfusions, carried out by Ian Hufton, were contaminated with the hepatitis C virus, a chronic disease that affects liver function and he became infected with the disease as an infant.

The plaintiff's lawyers, Nicholl and Company, claim that the Red Cross Blood Service was negligent for not screening donated blood for the virus by checking for tell-tale elevated liver enzyme levels, or carrying out other checks. It is further claimed that the blood service failed to warn potential donor recipients that the blood might contain the virus and there was a danger of transmission.

The man's lawyers claim that the hospital was negligent in not applying any of the checks to donated blood supply, in not using neo-natal transfusions as a technique of last resort and in not obtaining informed consent for the procedure. He is seeking undisclosed damages from the Blood Service and the hospital.

The man says he must now face the prospect of decreased life expectancy and risks developing classic hepatitis C related conditions such as liver cancer or cirrhosis of the liver.

Shared insulin pens can transmit blood-borne pathogens

<http://www.modernmedicine.com>

Key Points

- 2,114 diabetic patients at the William Beaumont Army Medical Center in El Paso may have been exposed a blood-borne disease as a result of incorrect procedures used during insulin administration.
- Up to 15 patients at a second facility may be at similar risk for similar reason.
- FDA issued a Healthcare Professional Sheet and an FDA news release on March 19 alerting healthcare professionals and patients to the dangers involved in the sharing of insulin pens, cartridges, and needles.

Insulin pens are pen-shaped injector devices designed for patient self-administration of insulin. The pens are intended for use by a single patient only. The pens have a reservoir or cartridge that can deliver multiple doses of insulin; however, a new needle must be used with each injection. Patients should never share insulin pens, cartridges, or needles. If the insulin pens, cartridges, or needles are shared, there is a risk of transmission of blood-borne pathogens, such as hepatitis B (HBV), hepatitis C (HCV), and human immunodeficiency virus (HIV).

The FDA has received information that insulin pens may have been shared among many patients in one hospital and among a smaller number of patients in another hospital.

A press release from the William Beaumont Army Medical Center, El Paso, Texas, announced that 2,114 diabetic patients admitted to the medical center between August 2007 and January 2009 may be at risk for developing a blood-borne disease as a result of incorrect procedures employed during the administration of insulin through insulin pens.

In August 2007, the medical center staff began using the insulin pens to administer doses of insulin to patients. In this incident, although new sterile needles were used on all patients with each injection, the same pen may have been used on more than one patient. The medical center staff planned to contact all 2,114 diabetic patients and offer screening for blood-borne diseases such as HBV, HCV, and HIV.

The investigation also revealed that the insulin pen may not have been used properly at a second facility and up to 15 patients may be at risk for developing a blood-borne disease. Some of the patients who may have been exposed have reportedly tested positive for hepatitis C. However, additional testing is needed to determine whether the hepatitis infection occurred through the sharing of insulin pens, or whether those who tested positive had cases of previously undiagnosed hepatitis C.

Following receipt of this information, the FDA issued a Healthcare Professional Sheet and an FDA News Release on March 19, 2009, to alert healthcare professionals and patients that insulin pens and cartridges should never be shared between patients. As stated above, the sharing of insulin pens, cartridges, or needles will result in risk of transmission of HBV, HCV, HIV, or other blood-borne pathogens.

We would like to take this opportunity to highlight the following important safety information that was communicated in the aforementioned Healthcare Professional Sheet:

- Insulin pens containing multiple doses of insulin are meant for use by a single patient only;

they are not to be shared between patients.

- Identifying the insulin pen with the name of the patient and other patient identifiers provides a mechanism for verifying that the correct pen is used on the correct patient and can help minimize medication errors. Ensure that the identifying patient information does not obstruct the dosing window or other product information such as the product name and strength.
- Be aware that the likelihood of sharing insulin pens and cartridges increases when the pens are not marked with the patient name or other identifiers.
- The disposable needle should be ejected from the insulin pen and properly discarded after each injection. A new needle should be attached to the insulin pen before each new injection.
- The same risk of transmission of blood-borne pathogens may exist with shared use of any reusable injection device.
- Hospitals and other healthcare facilities should review their policies and educate their staff regarding safe use of insulin pens.

Pharmacists play an important role in patient care. When counseling, pharmacists should instruct patients that insulin pens are designed for use by a single patient and should never be shared with another patient. Each pen has a reservoir or cartridge that contains enough insulin for a patient to self-administer several doses or injections. Patients should be reminded to remove and properly dispose of the used needle after an injection. The pen cap should be placed on the pen device between each use. Storing the pen without the used needle will help prevent air, blood, and/or skin material from migrating into the insulin reservoir or cartridge from the needle. Instruct patients that although the insulin reservoir or cartridge contains anti-microbial agents, these agents are effective only against bacteria and are not effective against viruses, such as HBV, HCV, and HIV.

Although these recent incidents occurred at hospitals, the risk of transmission of blood-borne diseases can occur in any setting, such as long-term-care facilities, outpatient clinics, and even the home, if family members do not follow safe injection practices.

If you become aware of medication errors or other adverse events involving insulin pens, please report them to the FDA's MedWatch program available online at <http://www.fda.gov/medwatch/>.

Scott Dallas, RPh, USPHS, is Safety Evaluator, Division of Medication Error Prevention and Analysis, Office of Surveillance and Epidemiology, FDA. Carol Holquist, RPh, USPHS, is Director, Division of Medication Error Prevention and Analysis, Office of Surveillance and Epidemiology, FDA.

May 31, 2009

Hepatitis C victims face many obstacles

<http://www.timescolonist.com>

By Jessica Chan

'Silent epidemic' carries stigma of drug users

Hepatitis C is often referred to as a silent epidemic. It has few initial symptoms, but its long-term effects are grave. Progressive fibrosis. Cirrhosis. Liver cancer. Not to mention the daily difficulties of living with a progressive illness.



May was hepatitis month, yet little information circulated through the mainstream about this devastating blood-borne liver disease, despite the fact that it affects one to two per cent of the Canadian population. That's up to 600,000 people, with 300 new cases diagnosed each month.

There is no certain cure for hepatitis C, although an accepted but costly treatment is available. It is most often transmitted via shared IV drug needles, cocaine pipes and other equipment, pre-1990 blood transfusions or blood products, tattoos or piercings with unhygienic needles or piercing guns or needle-prick accidents. The hepatitis C virus slowly but relentlessly attacks various parts of the body, particularly the liver.

Those who are diagnosed with hepatitis C might have been initially infected years ago, making one wonder how they got it in the first place. Unfortunately, hepatitis C has been stigmatized because some people contract it through the use of drugs.

In fact, many people who contract hepatitis C do not publicly admit they have it out of fear others will scrutinize the way they contracted it. Although use of unhygienic equipment when using illicit drugs is a method of transmission, hepatitis C is a blood borne virus that can survive for up to 16 hours, but not more than four days, on surfaces outside the body.

Any instrument shared between two people, where open wounds might be exposed and one person is infected, could result in an exposure to hepatitis C. For example, an activity as minor as sharing toothbrushes could lead to exposure to hepatitis C. Gums often bleed, causing blood to be transferred onto the toothbrush. If someone else uses that same toothbrush and has open wounds, he or she could be exposed to hepatitis C if the previous user had it.

Once diagnosed with hepatitis C, people face many obstacles.

First, they must face the scrutiny of those around them and the stigma associated with blood-borne diseases.

They then have to engage with the medical system in order to get treatment.

And they might have to endure an estrangement from family and friends who treat them differently. Many people do not understand how hepatitis C is spread and will avoid the person altogether.

Unfortunately, there is no vaccine for hepatitis C as there is for hepatitis A and B. There is a silver lining for those with hepatitis C, though. Treatment does exist in the form of weekly injections of interferon and twice daily pills of ribavirin. Success rates can range from 40 to 90 per cent, depending on which strain of hepatitis C you have and adherence to the treatment.

People who opt not to participate in treatment may continue to live healthy lives with a few simple lifestyle changes, like abstaining from drinking and exercising regularly.

It is important to get tested if you believe you have ever been exposed to hepatitis C. The earlier you find out, the quicker you can take action to live a healthier lifestyle.

It's also important to remember that hepatitis C does not discriminate and neither should we.

Jessica Chan is acting executive director of Hep CBC. For more information on hepatitis C please visit hepcbc.ca or avi.org.

June 1, 2009

"Gene Silencing" May Improve Treatment of a Deadly Complication of Liver Disease

<http://www.medicalnewstoday.com>

A technique that "silences," or turns off, genes shows promise as a potential new treatment for liver fibrosis - the disease that leads to cirrhosis - scientists in Tennessee are reporting. Their study is scheduled for the June 1 issue of ACS' *Molecular Pharmaceutics*, a bi-monthly journal. Cirrhosis is the 12th leading cause of death in the United States.

Ram Mahato and colleagues note that fibrosis involves build-up of scar tissue in the liver from chronic liver damage caused by hepatitis, alcohol abuse, toxins, or other factors. Advanced fibrosis can lead to cirrhosis, a condition in which the liver becomes so severely damaged that patients may require a transplant. There is no effective treatment, and patients urgently need new medications. Scientists believe one may emerge from the fascinating discovery that a protein called TGF-beta 1 triggers liver inflammation and that blocking the protein may help.

The researchers designed 10 chemically synthesized substances, termed siRNAs, with the ability to block or "silence" the TGF-beta 1 gene in the liver. When put into rat liver cells, the "gene silencers" decreased levels of type 1 collagen whose excessive production leads to fibrosis, as well as two other substances known to trigger liver inflammation, by almost 50 percent. The results suggest that gene silencing may be "an efficient and more specific approach for therapy of liver fibrosis," the report states.

Source: American Chemical Society

Innovative Ultrasound Provides Cutting Edge Acoustic Radiation Force Impulse Technology for Liver Imaging

<http://www.medicalnewstoday.com>

The Radiology department at King's College Hospital is now benefiting from enhanced ultrasound image quality and optimised workflow following the installation of an ACUSON S2000™ from Siemens Healthcare. The hospital also uses the S2000's Virtual Touch™ application for Acoustic Radiation Force Impulse (ARFI) imaging to assist with scanning the liver.

The S2000 is a next generation ultrasound system offering superior image quality to improve diagnostic confidence, plus ensures user and patient comfort through its adaptive ergonomic design. It is being used at the hospital predominantly for contrast ultrasound of the liver and testicular cases as well as more general scanning.

The Virtual Touch application uses acoustic energy to compress tissue and provide qualitative

and quantitative assessments of deep tissue stiffness. This is particularly beneficial for examinations of the liver and is also a quick, non-invasive solution for diagnosis.

The system includes an 18L6 HD transducer for use in testicular ultrasound examinations at the hospital. It has a long cable for ease of use and features an ElastoGrip™ ergonomic grip coating that improves control by reducing grip force and operator fatigue.

"ARFI provides a high quality level of imaging when conducting ultrasound scans of the liver," states Paul Sidhu, Consultant Radiologist at King's College Hospital. "As the primary user of the system, I have found the S2000 to be comfortable as well as easy to use and its portability has served as a great benefit to the hospital."

"We are very pleased that King's College Hospital has installed one of our leading ultrasound systems," states Yianni Kiromitis, Regional Sales Manager, Ultrasound at Siemens Healthcare. "The S2000 is a real step forward for ultrasound imaging as it offers next generation functionality for all disciplines and expands the range of techniques offered to patients."

The S2000 is compact, lightweight and portable providing ultimate user comfort. The controls are within easy reach of the operator and its flexible arm and flat panel display ensure clear image quality in all lighting environments. The system draws together the latest imaging innovations including 2D, 3D, Colour and Pulse-wave Doppler and 4D images to optimise workflow and simplify examinations.

Source: Siemens Healthcare

Phase 3 Trial Initiated To Evaluate Combination Therapy Of Nexavar(R) And Tarceva(R) In Patients With Liver Cancer

<http://www.medicalnewstoday.com>

Bayer HealthCare LLC., Onyx Pharmaceuticals, Inc. (Nasdaq: ONXX), OSI Pharmaceuticals, Inc. (Nasdaq: OSIP) and Roche today announced the initiation of a Phase 3 trial examining Nexavar(R) (sorafenib) tablets in combination with Tarceva(R) (erlotinib) tablets as a potential new treatment option for patients with advanced hepatocellular carcinoma (HCC), or primary liver cancer.

The SEARCH (Sorafenib and erlotinib, a randomized trial protocol for the treatment of patients with hepatocellular carcinoma) trial aims to further build on data from the Phase 3 SHARP trial, which demonstrated that Nexavar significantly extended overall survival in patients with unresectable liver cancer by 44 percent (HR=0.69; p-value=0.0006). Based on the strength of these data, Nexavar was approved for the treatment of patients with unresectable HCC in the United States and in Europe for the treatment of HCC. Nexavar is currently approved in more than 70 countries for the treatment of HCC, including China where more than half of all liver cancer cases worldwide occur each year.

"Nexavar is the only approved targeted therapy with efficacy and tolerability in liver cancer," said Dimitris Voliotis, MD, vice president, Nexavar Clinical Development, Bayer HealthCare Pharmaceuticals. "We look forward to seeing the potential of combining Nexavar with another

effective cancer treatment, Tarceva, in treating this disease and further extending the lives of patients."

"This study will enable us to learn whether combining two oral targeted therapies, Nexavar and Tarceva, can improve survival in a disease that is difficult to treat since most patients are diagnosed at an advanced stage," said Karsten Witt, M.D., Vice President, Clinical Development Oncology and Drug Safety, OSI Pharmaceuticals. "We are pleased to collaborate with Roche, Bayer and Onyx to explore Tarceva in hepatocellular carcinoma, a new disease area which if successful, has the potential to expand the use of Tarceva beyond its current indications in second/third-line non-small cell lung cancer and first-line pancreatic cancer."

About the Phase 3 Study

The international multicenter randomized placebo-controlled Phase 3 study is expected to enroll approximately 700 patients with advanced liver cancer. The study will examine whether Nexavar in combination with Tarceva prolongs survival as compared to Nexavar alone. The primary endpoint of the study is overall survival and the secondary endpoints are safety, time to radiographic progression, disease control rate and patient-reported outcome.

Patients will be randomized to receive either 400 mg of Nexavar twice daily and 150 mg of Tarceva once daily or 400 mg of Nexavar twice daily with matching placebo. The study will be conducted at more than 95 sites in North America, Europe and the Asia-Pacific region.

About Hepatocellular Carcinoma

Hepatocellular carcinoma is the most common form of liver cancer and is responsible for about 90 percent of the primary malignant liver tumors in adults.(1,2) Liver cancer is the sixth most common cancer in the world and the third leading cause of cancer-related deaths globally.(3) More than 600,000 cases of liver cancer are diagnosed worldwide each year (more than 400,000 in China, South Korea, Japan and Taiwan, 54,000 in the European Union, and 15,000 in the United States) and the incidence is increasing.(3,4) In 2002, approximately 600,000 people died of liver cancer including approximately 370,000 in China, South Korea and Japan, 57,000 in the European Union, and 13,000 in the United States.(3)

Nexavar's Differentiated Mechanism

Nexavar, an oral anti-cancer therapy, is currently approved in more than 70 countries for liver cancer and in more than 80 countries for the treatment of patients with advanced kidney cancer. Nexavar targets both the tumor cell and tumor vasculature. In preclinical studies, Nexavar has been shown to target members of two classes of kinases known to be involved in both cell proliferation (growth) and angiogenesis (blood supply) - two important processes that enable cancer growth. These kinases included Raf kinase, VEGFR-1, VEGFR-2, VEGFR-3, PDGFR-B, KIT, FLT-3 and RET.

Nexavar, which is co-developed by Bayer Healthcare Pharmaceuticals and Onyx Pharmaceuticals, Inc., is being evaluated by the companies, international study groups, government agencies and individual investigators as a single agent or combination treatment in a wide range of other cancers, including breast cancer, lung cancer, ovarian cancer, colorectal cancer, and as an adjuvant therapy for kidney cancer and liver cancer.

About Tarceva

Tarceva is a once-a-day pill that targets the EGFR pathway. Tarceva is designed to inhibit the tyrosine kinase activity of the EGFR signaling pathway inside the cell, one of the critical growth factors in NSCLC and pancreatic cancers. Tarceva is indicated as a monotherapy for patients with locally advanced or metastatic NSCLC whose disease has progressed after one or more courses of chemotherapy. Results from two multicenter, placebo-controlled, randomized Phase 3 trials conducted in first-line patients with locally advanced or metastatic NSCLC showed no clinical benefit with the concurrent administration of Tarceva with platinum-based chemotherapy (carboplatin and paclitaxel or gemcitabine and cisplatin) and its use is not recommended in that setting.

In pancreatic cancer, Tarceva is indicated in combination with gemcitabine for the first-line treatment of patients with locally advanced pancreatic cancer, pancreatic cancer that cannot be surgically removed or pancreatic cancer that has spread to distant body organs.

Liver disease 'shrunk' by blood-pressure drug

<http://www.eurekalert.org>

A blood-pressure medicine has been shown to reverse the effects of early-stage liver failure in some patients.

Newcastle University researchers analysed a small clinical trial of losartan, a drug normally prescribed for hypertension, on 14 patients in Spain, who had Hepatitis C.

The illness was at an advanced stage causing fibrosis - scarring in the liver - which would usually have progressed to liver failure.

Half of the patients in the trial saw the scars in their liver shrink allowing the organ to repair itself.

Professor Derek Mann from Newcastle University said: "At the moment we have no proven effective way of treating people with chronic liver disease other than transplantation. This early stage trial has shown that we can shrink liver scarring in some patients and shows promise for a treatment that could make a huge difference to the lives of thousands of people."

The team whose work is published today in *Gastroenterology*, say this early stage trial is promising and they now want to carry out several much larger studies initially involving patients with liver disease caused by obesity and then later alcohol, hereditary and autoimmune diseases.

Mechanism

Liver damage, known as fibrosis, is caused by the unwanted accumulation of excess fibrous connective tissue which is produced and maintained by a specialised cell, the liver myofibroblast.

In chronic liver disease a signalling pathway is created that instructs the liver myofibroblast to stay alive and proliferate. It is this pathway that then causes scar tissue to accumulate, creating the liver damage.

Work carried out in rat and mouse models allowed the researchers to study what was happening inside the liver when losartan, an angiotensin II receptor antagonist drug, was present.

Researchers believe that the drug blocks the signalling pathway so that the liver myofibroblasts die, removing the source of scar tissue. As the scar tissue breaks up, the damaged area of the liver is repaired by the body.

In this research, funded by the Medical Research Council and the British Liver Trust, the Newcastle University researchers discovered a biological marker, NF-kB, was crucial for the activities of scar-forming cells.

Tests on their livers revealed that, before treatment with losartan, half of the patients had a high level of the biomarker NF-kB. After treatment, the level fell indicating that losartan is able to switch off NF-kB with the result that scars are no longer produced or maintained, but instead shrink.

Professor Mann said: "By measuring the amount of active NF-kB in the liver from a biopsy sample, we may be able to tell which patients will benefit from treatment with losartan or similar drugs such as ACE inhibitors. This may prove to be a new treatment for up to half of all liver patients."

The trial was carried out with patients at the Liver Unit, Institut Clinic de Malalties Digestives i Mataboliques, Hospital Clinic, Insitut d'Investigacions Biomediques August Pi i Sunyer, Barcelona, Spain.

People with liver disease caused by being overweight – though fatty liver disease or NASH (Nonalcoholic Steatohepatitis) – and who are interested in taking part in a future clinical trial should leave their details on tel: 0191 2231900

Paper:

Angiotensin II activates I κ B kinase phosphorylation of RelA at Ser536 to promote myofibroblast survival and liver fibrosis

Authors:

Fiona Oakley, Victoria Teoh, Gemma Ching-A-Sue, Ramon Bataller, Jordi Colmenero, Julie R Jonsson, Aristides G Eliopoulos, Martha R Watson, Derek Manas, Derek A Mann.

New screening test could reduce high mortality rates in patients with liver cancer

<http://www.hospitalnews.com>

Christopher Needles

Dr. Jorge Filmus is developing a blood test that could detect primary liver cancer early on, allowing doctors to remove the cancer before it becomes dangerous.

Primary liver cancer is one of the most common types of cancer in the world. Unfortunately, it is usually diagnosed far too late for treatment. As a result, it is the third most common cause of

cancer-related death worldwide. Primary liver cancer occurs when tumours develop in the liver itself and have not spread from other parts of the body.

Dr. Jorge Filmus is a Senior Scientist at Sunnybrook Health Sciences Centre in Toronto. He has spent much of the last decade developing a revolutionary new test to proactively screen patients for liver cancer. This test would find tumours while they are still small enough to be removed, significantly reducing the disease's high mortality rates.

“There is currently no effective cure for advanced liver cancer,” says Filmus. “By the time patients feel symptoms of the disease, the cancer has spread and there is almost no chance of curing it. But if we can use this test to detect a tumour when it is small, before it has spread, a surgeon can then go in and easily remove it. At that point a patient can make a full recovery.”

Filmus' test uses antibodies to detect the presence of the biomarker glypican-3 in a patient's blood. Patients at risk for liver cancer are people living with chronic hepatitis B or C or those with cirrhosis of the liver. They would have a blood test every six months to one year. Detection of glypican-3 would indicate that liver cancer is probably present in the body. Doctors could then locate the tumour and remove it.

Currently, most doctors use the alpha-fetoprotein (AFP) blood test or an ultrasound to diagnose the disease. “Neither are very good at detecting small lesions, which are the ones that we want to detect,” Filmus explains. “Looking for Glypican-3 is a good way to detect liver cancer because it is not produced by a normal liver. It is also not produced by a liver infected with hepatitis virus, or a liver that has non-cancerous lesions. Glypican-3 is only produced by malignant cells.”

The test could be easily adopted worldwide: it is simple and straightforward to perform and the technology is quite minimal. Filmus estimates that the final test could cost as little as \$25 per patient. “The test is a very simple one that any clinical laboratory, even in developing countries, could perform with ease. Patients won't have to go to a major hospital to get it.” An estimated \$1 billion is spent each year worldwide on screening for liver cancer; this test could provide a better and inexpensive way to detect liver cancer at an early stage.

Chronic hepatitis leads to cirrhosis of the liver, which makes the liver prone to cancer. About 80 per cent of people who develop primary liver cancer have chronic hepatitis B or C. While hepatitis rates in North America are low compared to other parts of the world, the rate here has doubled in the last 15 years. Over 300 million people worldwide currently live with chronic hepatitis.

“We know who is at high risk of developing liver cancer. So we have a target population for screening that is quite large. Even if we make a conservative guess and say we will only be able to detect liver cancer at an early stage in 0.1 per cent of these people tested with the glypican-3 blood test, we're still talking about saving many lives.”

The Ontario Institute for Cancer Research (OICR) recently awarded Dr. Filmus' lab \$280,000 to help commercialize the test for distribution. “Dr. Filmus' research could change how liver cancer is diagnosed,” says Dr. Tom Hudson, OICR's President and Scientific Director. “We could see this disease go from being one of the most deadly to one that, with the proper care, can be effectively managed. We are happy to support the development of this test and help to get it to

patients sooner.”

Filmus says there is still some work to be done before the test is ready for clinical use. His lab is working with two companies, BioMosaics and Amorfix Life Sciences, to optimize the sensitivity of the test. “It’s one thing to have this work in a lab, but in an actual clinical laboratory it is much more complicated,” Filmus says. “You don’t want small errors to lead to misdiagnoses. But we are optimistic. We have identified new antibodies that will allow us to develop a better test.

“Better hepatitis vaccines may ultimately prevent much liver cancer,” Filmus adds, “but until that happens we need to diagnose it at an early stage before it spreads and becomes incurable.” That may sound like a small difference, but it’s a difference that could ultimately save millions of lives around the world.

Christopher Needles is a Communications Officer at the Ontario Institute for Cancer Research

June 2, 2009

SAFE biopsy is a validated method for staging liver fibrosis in Hep C

<http://www.gastrohep.com>

SAFE biopsy is a validated method for large-scale staging of liver fibrosis in chronic hepatitis, finds the latest issue of *Hepatology*.

The staging of liver fibrosis is pivotal for defining the prognosis and indications for therapy in Hepatitis C.

Although liver biopsy remains the gold standard, several noninvasive methods are under evaluation for clinical use.

Dr Giada Sebastiani and colleagues from Italy validated the recently described sequential algorithm for fibrosis evaluation biopsy.

The biopsy detects significant fibrosis and cirrhosis by combining the AST-to-platelet ratio index and Fibrotest-Fibrosure, thereby limiting liver biopsy to cases not adequately classifiable by noninvasive markers.

The researchers enrolled Hepatitis C virus patients in 9 locations in Europe and the United States.

The diagnostic accuracy of safe biopsy versus histology, which is the gold standard, was investigated.

The reduction in the need for liver biopsies achieved with safe biopsy was also assessed.

Safe biopsy identified significant fibrosis with 90% accuracy, and reduced the number of liver biopsies needed by 47%.

The team found safe biopsy had 93% accuracy for the detection of cirrhosis, obviating 82% of

liver biopsies.

A third algorithm identified significant fibrosis and cirrhosis simultaneously with high accuracy and a 36% reduction in the need for liver biopsy.

The patient's age and body mass index influenced the performance of safe biopsy, which was improved with adjusted Fibrotest-Fibrosure cutoffs.

The team found that 10% of cases had discordant results for significant fibrosis with safe biopsy versus histology, whereas 8% of cases were discordant for cirrhosis detection.

The research team found that 71 of the former cases and 56 of the latter cases had a Fibroscan measurement within 2 months of histological evaluation.

Fibroscan confirmed safe biopsy findings in 83% and 75%, respectively.

Dr Sebastiani's team concluded, "Safe biopsy is a rational and validated method for staging liver fibrosis in hepatitis C with a marked reduction in the need for liver biopsy."

"It is an attractive tool for large-scale screening of Hepatitis C virus carriers."

Hepatology 2009; 49(6): 1821-7

HCV Viral Load Decline at Day 2 of Interferon-based Therapy Predicts Sustained Response, Explains Poorer Outcomes in African-Americans

<http://www.hivandhepatitis.com>

Liz Highleyman

Declines in hepatitis C virus (HCV) viral load as early as 2 days after starting interferon-based therapy can help predict which individuals will achieve sustained virological response (SVR), and may help explain why different racial/ethnic groups respond differently to treatment, according to a study in the April 15, 2009 *Journal of Infectious Diseases*.

Past research has established that people of African descent do not respond as well as Caucasians to interferon-based therapy for hepatitis C; people of Asian descent tend to respond better than other groups, while data are mixed for Latino/Hispanic patients.

The Virahep-C trial, sponsored by the National Institutes of Health, was designed to look at factors associated with differences in hepatitis C treatment response, especially disparities between whites and African-Americans.

A total of 401 previously untreated genotype 1 chronic hepatitis C patients (205 Caucasian, 196 African-American) were treated with 180 mcg/week pegylated interferon alpha-2a (Pegasys) plus 1000-1200 mg daily weight-adjusted ribavirin, initially for 24 weeks. Those who did not achieve undetectable HCV RNA at this point stopped therapy, while responders continued

treatment for a total of 48 weeks.

In the present analysis, Jay Hoofnagle from the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) and colleagues assessed early changes in HCV RNA levels among Virahep-C participants. The analysis was restricted to 341 patients who completed the first 28 days of therapy without dose modification (the point at which rapid virological response, or RVR, is assessed).

Results

- HCV RNA levels decreased in almost all participants, but the amount of decline varied markedly from patient to patient.
- Differences in HCV RNA decline between whites and African-Americans reached statistical significance by day 2 of treatment.
- At day 28, 22% of Caucasians had undetectable HCV RNA compared with 12% of African-Americans.
- The overall decrease in HCV RNA at day 28 predicted SVR at least as well as first-phase or second-phase viral kinetics.
- Factors associated with a smaller decline in HCV RNA from baseline to day 28 included:
 - African-American race;
 - Higher initial HCV RNA level;
 - More severe hepatic fibrosis;
 - Higher body weight.
- African American patients whose 28 day decline in viral load was similar to that of white patients were still less likely to achieve SVR.

These findings led the researchers to suggest that racial differences in response to standard anti-HCV therapy are likely related to biological -- likely genetic -- differences in how the body responds to interferon.

"The underlying cause of virological non-response and the reasons why it is more common among African Americans than Caucasian Americans are not clear," the study authors wrote. "[T]he current analyses demonstrated that these differences are fundamentally biologic and become apparent within 24 to 48 hours of starting therapy."

In conclusion, they wrote, "These results suggest that racial differences in the response to antiviral therapy are due to greater unresponsiveness to intracellular actions of interferon in African American individuals and that standard doses of peginterferon and ribavirin may be suboptimal for patients with higher body weights."

Previously presented Virahep-C research has looked at associations between racial differences in treatment response and interferon pharmacokinetics, genetic differences in interferon signaling, and major histocompatibility genes.

In an editorial accompanying Hoofnagle's report, Andrew Tai and Raymond Chung from Massachusetts General Hospital wrote that this analysis "demonstrates that the low rates of SVR in African American patients in response to interferon-based therapy appear to result, in large part, from impaired early viral kinetics. Further studies are necessary to uncover the relevant mechanisms that underlie this defect in interferon signaling with the hope that such mechanisms

can be manipulated to restore interferon responsiveness in the otherwise nonresponsive host."

If poorer outcomes among African-Americans are shown to be due to reduced responsiveness to interferon, differences in treatment response might diminish with the use of investigational antiviral agents that directly target various stages of the HCV life cycle rather than modulating immune function.

Liver Disease Research Branch, Division of Digestive Diseases and Nutrition, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, MD; Division of Hepatology, University of Maryland School of Medicine, Baltimore, MD; Departments of Biostatistics and Epidemiology, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, PA; Division of Gastroenterology and Hepatology, New York-Presbyterian Medical Center, New York, NY.

6/02/09

References

JH Hoofnagle, AS Wahed, RS Brown, and others. Early Changes in Hepatitis C Virus (HCV) Levels in Response to Peginterferon and Ribavirin Treatment in Patients with Chronic HCV Genotype 1 Infection. *Journal of Infectious Diseases* 199(8):1112-1120. April 15, 2009

AW Tai and RT Chung. Racial Differences in Response to Interferon-Based Antiviral Therapy for Hepatitis C Virus Infection: A Hardwiring Issue? *Journal of Infectious Diseases* 199(8): 1101-1103. April 15, 2009.

NHS trust defends delay over HIV and hepatitis warnings

<http://www.bournemouthcho.co.uk>

HEALTH chiefs in Bournemouth have defended their decision to wait months before telling thousands of NHS dental patients they could have been exposed to HIV or hepatitis.

NHS Bournemouth and Poole has sent out letters to around 3,500 people and set up a telephone advice line after staff at the Poole Lane Dental Practice in Kinson raised concerns over a locum dentist's infection control. The locum worked there between January and October last year and is also said to have put thousands at risk while working in Bristol between 2003 and 2007.

He is no longer practising as a dentist in the UK.

Dr Adrian Dawson, director of public health for Bournemouth and Poole, said immediate action had been taken when the alarm was raised last autumn, but it had taken some time to identify patients potentially put at risk.

He added: "Patient safety is our number one concern and the most important action was to remove the dentist from delivering patient care, which was done swiftly.

"There had to be a careful decision made regarding the timing of contacting patients – too soon would have risked tests missing some infections, which can incubate for up to six months."

The locum dentist, who has not been named, was taken on to provide cover for Abbasali Tamali, who is currently suspended pending a General Dental Council fitness to practice hearing over charges to NHS patients. Another dentist who practised from the same address under a separate NHS contract is also under investigation.

Dr Dawson said it had taken some time to identify patients who may have been put at risk by the locum. Expert Health Protection Agency advice had been followed over when to tell them. Up to half are expected to take up the offer of blood tests.

Dr Sue Bennett, director of the Dorset Health Protection Unit, stressed that HIV was very difficult to transmit via instruments and that good treatments were now available for hepatitis B and C.

One of the patients contacted said: "My last treatment was late last year. I'm surprised it's taken this long."

Steve Smith of Redhill said he and his five-year-old son were booked in for blood tests on Wednesday. "I'm definitely feeling worried. It's quite shocking because kids are involved. It does seem to have taken a long time from October to now. We should have been told straight away that this might have been a problem."

Hep "C" Scare prompts new laws

<http://www.ktnv.com>

Nevada State health officials have some good things to say about some new laws sparked by the Hepatitis "C" outbreak here in the Las Vegas Valley.

Governor Jim Gibbons signed five laws that should make it harder for anything "similar" to happen again.

More than 50,000 patients had to be notified that they might have been exposed to Hepatitis "C" while being treated at two outpatient clinics that didn't use needles properly.

One of the new law requires unannounced inspections every year, instead of every three to six years.

Meantime, another new law helps to protect medical whistle blowers.

Valeant Pharmaceuticals Reports Encouraging Final Results With Taribavirin Phase IIb Study

<http://www.medicalnewstoday.com/>

Valeant Pharmaceuticals International (NYSE: VRX) reported final results for its Phase IIb dose-finding clinical trial for taribavirin, a prodrug of ribavirin which is in development for the treatment of chronic hepatitis C in conjunction with a pegylated interferon. The study in

treatment naive genotype 1 infected subjects was of standard design, consisting of 48 weeks of treatment with a 24-week follow-up period. It explored three weight-based doses of taribavirin: 20 mg/kg, 25 mg/kg and 30 mg/kg vs. ribavirin 800-1400 mg/day. Throughout the 72-week trial, all doses of taribavirin demonstrated comparable efficacy (sustained virologic response (SVR)) to ribavirin with consistently lower levels of anemia. In addition, relapse rates in the 25 mg/kg and 30 mg/kg arms were comparable with the ribavirin arm; supporting the premise that higher dose weight-based taribavirin may be as effective as weight based ribavirin. Valeant plans to present the full final data at the American Association for the Study of Liver Disease (AASLD) later this year.

"The final results of this Phase II study are promising and imply that comparable efficacy with taribavirin can be achieved when compared to ribavirin," stated Fred Poordad, M.D., Chief of Hepatology at the Center for Liver Disease and Transplantation, Cedars-Sinai Medical Center, Los Angeles, CA. "As is known for ribavirin, low doses are associated with a high relapse rate and, except for the lowest dose with taribavirin, relapse rates are also comparable to ribavirin. The safety of this ribavirin analog is of particular relevance in the evolving era of small molecule therapies as anemia appears to be more problematic."

"We are very pleased with the results from this dose finding study which confirms that taribavirin could replace ribavirin as a cornerstone in the treatment of hepatitis C, but with the advantage of less anemia," said J. Michael Pearson, chairman and chief executive officer. "These encouraging results, coupled with Schering-Plough's option agreement for a license in Japan, could offer new alternatives for patients suffering from this disease and we will continue to pursue additional licensing and partnering opportunities in order to maximize this compound's potential."

The most common adverse events during treatment were fatigue, nausea, flu-like symptoms, headache and diarrhea. The incidence rates for these adverse events among treatment arms were generally comparable except with respect to diarrhea, where incidence of diarrhea was approximately twice as common in patients receiving taribavirin compared to patients receiving ribavirin. However, the diarrhea was generally mild and not treatment limiting for taribavirin or ribavirin patients.

About Taribavirin

Taribavirin is an investigational compound that has not been found by the Food and Drug Administration (FDA) or any other regulatory agency to be safe or effective in the diagnosis, mitigation, treatment or cure of any disease or illness. It may not be sold or promoted in the United States unless and until approved for marketing by the FDA. Similar restrictions apply in other countries.

About Study 204

The Phase IIb trial is a U.S. multi-center, randomized, parallel, open-label study in 278 treatment-naïve, genotype 1 patients evaluating taribavirin at weight-based doses of 20 mg/kg, 25 mg/kg, and 30 mg/kg per day in combination with pegylated interferon alfa-2b. The control group was administered weight-based dose ribavirin (800/1000/1200/1400mg daily) and pegylated interferon alfa-2b. Overall treatment duration is 48 weeks with a post-treatment follow-up period of 24 weeks.

In the Phase IIb study (previously disclosed as Study 204), 278 treatment naive, genotype 1 patients were randomized with the following patient demographics: mean age 48.8 yrs, 61.1% male, 30% African-American or Latino, 80.7% viral load $\geq 400,000$ IU/mL and 82.1 kg mean weight.

Former Drug Czar Urges Awareness of Hepatitis C Reporting

<http://wjz.com>

Kellye Lynn

For more than 30 years, Mike Gimbel has served as a local authority on substance abuse. CBS

At his Baltimore County home, medals and photographs tell a story of miles crossed and challenges won. It's a fitting image of a 57-year-old former drug czar who survived years of substance abuse.

"It made me have courage. It made me fit in and all of a sudden I was one of the guys," said Mike Gimbel.

He says the partying started as a young teen, not long after his bar mitzvah.

"Within a very short period of time, I found myself smoking pot, taking LSD and cocaine and moving up the ladder," he said.

Rock bottom was a heroin addiction that ended after a seven-year stint at a drug treatment program in California. It was called Synonon and was very famous in the '60s and '70s.

He beat his addiction and then dedicated his life to helping others do the same. He was clean, an avid runner and quietly hoped he had escaped his old lifestyle without a scratch. He hadn't.

"About 10 years ago, I was diagnosed with having Hepatitis C. We know it came from my heroin use when I was 19 or 20 years old," Gimbel said.

Hepatitis C is a virus that causes inflammation of the liver and affects about 3.2 million people in the US. The chronic illness is most commonly spread by sharing needles or other equipment to inject drugs.

Although Gimbel feels great, his liver is scarred and he expects to begin treatment in the near future.

"Ultimately, this disease can lead to liver disease and ultimately you're looking at getting a liver transplant or even worse," he said.

He decided to reveal his illness now out of concern for the young people he encounters who are abusing drugs. He says they don't understand the consequences of drug use and hopes after hearing about his Hepatitis C, they will.

"They look at me and say, 'You look okay, you look healthy, I can do what you did.' Now I can comfortably say I'm not okay, I don't know what will happen. I may not live as long as I should have," he said.

He urges anyone who has used IV drugs to get tested for Hepatitis C.

Several well-known celebrities are also living with Hepatitis C, including actress Pamela Anderson, singers Natalie Cole, Naomi Judd and Steven Tyler of Aerosmith.

Patient at Methodist Dallas Medical Center Survives Amazing 54 Hours Without Liver

<http://sev.prnewswire.com>

DALLAS, June 2 /PRNewswire/ -- Doctors at The Liver Institute at Methodist Dallas Medical Center announced a successful transplant for a patient who was able to survive 54 hours without a liver. Fifty-seven year old Lois Eisemann was in the last stage of liver failure with less than 10 percent liver function and given 1 to 2 weeks to live when she received her first liver transplant at Methodist Dallas Medical Center. When her new liver failed to function and had to be removed, Ms. Eisemann survived 54 hours without a liver until a new one could be transplanted. Patients can usually survive for less than 24 hours without a liver.

Ms. Eisemann's survival without a liver for 54 hours was a medical challenge. "The non-function of a transplanted liver is a rare event and happens in less than 2 percent of the cases," says Transplant Surgeon Alejandro Mejia, MD, a physician on the medical staff at Methodist Health System. "However, when it does happen, fewer than 10 percent of the generally patients survive." Hepatologist Abdullah Mubarak, MD, also a physician on the medical staff at Methodist, adds, "Ms. Eisemann is a tenacious woman and has beat the odds. Her success story like many other liver transplants, however, does not happen without the tremendous efforts of every team member involved in the patient's care." Dr. Mubarak says that the graciousness of organ donors helps Ms. Eisemann and other organ recipients have a second chance at enjoying life again. "Her story highlights how organ donation is a true gift of life and should inspire more people to be organ donors," he says.

Ms. Eisemann's daughter Charmane Jackson says after the first liver failed, her mother's condition deteriorated rapidly. "We had decided to take her off life support and let her go," says Ms. Jackson. Fifteen minutes after making that decision, the unimaginable happened. Her mother's condition improved and she was able to survive until a new liver was found. After four months in the intensive care unit and three weeks of rehabilitation at Methodist Dallas, Lois Eisemann was able to go home.

Ms. Jackson says the doctors put their knowledge and expertise together and did an amazing job. She adds that the doctors, nurses and physical therapists at Methodist Dallas were her mom's biggest cheerleaders. "The fact that she is alive right now is a miracle from God," she says. Lois Eisemann says, "The doctors call me their miracle patient. I call them my heroes! They were always personable, pleasant and very attentive to work with. They always kept my spirits up and taught me to never give up or lose hope."

About the Liver Institute at Methodist Dallas

The Liver Institute is one of only three facilities in the Dallas area that perform adult liver transplants. In addition to liver transplantation, the Institute also offers comprehensive and multi-disciplinary care for liver disease. The program includes a hepatitis center; a general hepatology program; a liver tumor program; and a hepatobiliary and pancreatic disorder clinic. The Institute is currently involved in several research projects regarding treatments for patients with chronic Hepatitis C, Hepatitis B and other liver diseases.

Artificial Liver May Extend Lives

<http://www.newswise.com>

Newswise — The first artificial organ for liver patients that uses immortalized human liver cells, the Extracorporeal Liver Assist Device, or ELAD®, is a bedside system that treats blood plasma, metabolizing toxins and synthesizing proteins just like a real liver does.

NewYork-Presbyterian Hospital/Columbia University Medical Center is currently one of only a small number of hospitals in the U.S. offering this therapy to acute liver failure patients as part of ongoing clinical trials.

"These studies are looking at how well the system can extend patients' lives until a liver transplant becomes available. We're also interested to see if it can relieve the burden on the patient's liver enough so that it can regenerate and regain some of its function," says Dr. Robert Brown, site principal investigator, chief of the Division of Abdominal Organ Transplantation, and director of the Center for Liver Disease and Transplantation at NewYork-Presbyterian Hospital/Columbia University Medical Center. Dr. Brown is also the Frank Cardile Professor of Medicine and Pediatrics (in Surgery) at Columbia University College of Physicians and Surgeons.

The ongoing studies look at whether ELAD liver support improves survival compared with standard medical therapy. Patients are randomly assigned to receive either standard medical therapy plus the ELAD system, or standard medical therapy alone. Patients eligible for the study have life-threatening acute liver failure, often due to an infection. Another trial open to patients with liver failure due to drug overdose without underlying liver disease is expected to begin enrollment later this year.

The current trials expand on prior results from Phase 1 and 2 trials in the U.S. and U.K., and a pivotal, randomized, controlled clinical trial at two sites in China during 2006 and 2007. In the latter study, 69 patients with hepatitis B or C who had suffered ALF were treated with either ELAD or standard therapy. Thirty-day transplant-free survival rates were statistically higher in the ELAD group compared with the control.

Artificial livers have been attempted since the 1960s. Because previous designs didn't use human liver cells, they couldn't adequately filter toxins or create chemicals essential to metabolism and blood-clotting.

With the ELAD system, four 12-inch cartridges containing cells derived from human liver cells and fibers are mounted on a standard blood-pumping unit. The patient's blood plasma flows

inside of hollow fibers to allow appropriate two-way transfer of metabolites across the fiber membrane.

Liver transplantation is limited by the supply of donor livers. According to the United Network for Organ Sharing (UNOS), there were approximately 6,500 liver transplants performed in 2007; however, there are more than 16,000 patients on the waiting list. Each year only about one-third of those who need a donor liver will receive one, and many patients die while waiting.

Acute liver failure afflicts more than 30,000 Americans each year, including those with chronic liver diseases like hepatitis, as well as those whose livers were damaged, such as by taking too much acetaminophen pain medicine. If not treated effectively and promptly -- usually by transplantation -- patients experience organ failure, bleeding, coma and death. When a donor organ isn't available or if the patient is too sick for surgery, ELAD could be their only option.

ELAD is manufactured by Vital Therapies Inc. of San Diego, sponsors of the current clinical trial.

For more information, patients may call (866) NYP-NEWS.

June 3, 2009

Interferon and Ribavirin Second-Line Option for Hepatitis C

<http://www.medpagetoday.com>

By Crystal Phend, Staff Writer, MedPage Today

Reviewed by Zalman S. Agus, MD; Emeritus Professor
University of Pennsylvania School of Medicine and
Dorothy Caputo, MA, RN, BC-ADM, CDE, Nurse Planner

SAN FRANCISCO, June 2 -- Some hepatitis C patients who don't respond to standard therapy may get a second chance at eradication with daily interferon alfacon-1 (Infergen) plus ribavirin.

So found Bruce R. Bacon, M.D., of Saint Louis University, and colleagues in the randomized Daily-Dose Consensus Interferon and Ribavirin: Efficacy of Combined Therapy (DIRECT) clinical trial.

Among participants who failed initial treatment with pegylated interferon plus ribavirin, retreatment with the interferon alfacon-1 combination yielded sustained virologic response in 6.9% among the 9- μ g dose group and 10.7% in the 15- μ g dose group.

The response rates were particularly promising -- up to 31.6% -- in interferon-sensitive patients with low baseline liver fibrosis scores, the researchers reported in the June issue of *Hepatology*.

This strategy "can be considered for select patients with chronic hepatitis C virus who have failed to respond to prior treatment with pegylated interferon and ribavirin," they wrote.

Roughly half of patients with chronic hepatitis C fail to respond to their first course of the standard combination of pegylated interferon and ribavirin, the researchers noted.

No standard has yet emerged for second-line therapy, since simply repeating the same treatment yields response rates under 10%, they said.

"Some clinicians have used the 'watchful waiting' approach and are anticipating new antiviral therapies with either protease inhibitors or polymerase inhibitors," they wrote.

Others have tried switching pegylated interferon brands, extending the drug's duration, increasing doses, or maintenance dosing, they added.

The DIRECT trial, a registry trial for the combination in second-line therapy, tested high doses of daily consensus interferon in 487 nonresponders.

Interferon alfacon-1 is also known as consensus interferon because it is a recombinant molecule synthesized to contain the most common amino acids from various types of naturally occurring interferon alfa.

Participants were randomized for the first 24 weeks to no treatment or either 9 or 15 µg of subcutaneous interferon alfacon-1 per day, with 1,000 to 1,200 mg of oral ribavirin per day, depending on body weight.

After that period, control group patients were offered randomization to one of the two treatment dose groups.

Pooling the end-of-treatment results for these two phases of the trial, intent-to-treat analysis revealed virologic response in 14.7% of the 9-µg consensus interferon dose group and 18.5% in the 15 µg arm, followed by lower rates of sustained virologic response (defined as undetectable viral levels at least 24 weeks after treatment).

Pooled relapse rates were 52% and 42% among these responders, respectively.

Although the researchers warned that the study was not statistically powered to compare the dose groups, they noted that post hoc analysis revealed no difference in sustained virologic rates between the two (P=0.141).

While control group patients went untreated, none achieved sustained virologic response.

The best sustained virologic response rates were seen in patients with:

- A partial virologic response to their prior course of pegylated interferon treatment, with at least a 2-log₁₀ reduction in hepatitis C viral RNA (11% in the 9-µg group and 23% in the 15-µg group)
- Noncirrhotic patients with fibrosis scores of F0 to F3 at baseline (7.8% and 13.1%, respectively)
- Both interferon sensitivity and low fibrosis scores (10.7% and 31.6%, respectively)

Patients with cirrhosis did not appear to benefit from retreatment with consensus interferon and ribavirin unless they had at least a 1-log drop in viral levels on prior therapy, Dr. Bacon's group noted.

The researchers did not report number needed to treat and could not be contacted in time for publication.

But the consensus interferon-ribavirin combination appeared safe and well-tolerated for second-line therapy, they said.

The study was sponsored by InterMune and Valeant Pharmaceuticals International with additional support for the study publication from Three Rivers Pharmaceuticals.

Dr. Bacon reported conflicts of interest with Three Rivers, Roche, Bristol-Myers Squibb, Schering-Plough, Coley Pharmaceuticals, ISIS, Valeant, and GlaxoSmithKline.

Co-authors reported conflicts of interest for Schering-Plough, Roche, Three Rivers, Idenix, Valeant, Gilead Sciences, Biotex, and Vertex.

Primary source: *Hepatology*

Source reference: Bacon BR, et al "Retreating chronic hepatitis c with daily interferon alfacon-1/ribavirin after nonresponse to pegylated interferon/ribavirin: DIRECT results" *Hepatology* 2009; 49: 1838-46.

Hyperion Therapeutics Announces Results of Phase I Study in Patients with Liver Cirrhosis

<http://www.medicalnewstoday.com>

Hyperion Therapeutics, Inc. announced top-line results from a phase I study of **HPN-100** in patients with liver cirrhosis. The data were presented as part of the 2009 Digestive Disease Week meeting. The abstract is titled "Pharmacokinetic (PK) and Safety Analyses of a Novel Ammonia-Reducing Agent in Healthy Adults and Patients with Cirrhosis."

This open-label study was designed to determine the safety, tolerability, and PK and pharmacodynamic (PD) profiles of HPN-100 administered orally to subjects with hepatic impairment and cirrhosis and to subjects with normal hepatic function. A total of thirty-two subjects were enrolled, including twenty four with cirrhosis (eight each Child-Pugh score A, B, and C), and eight age- and gender-matched healthy subjects with normal hepatic function. Subjects received a single oral dose (100mg/kg/d) of HPN-100 on day 1, two doses of 100mg/kg on each of days 8-14 (total of 200mg/kg/d), and a single dose on day 15 (100mg/kg/d). In order to assess the effects of food on HPN-100 PK, the dose was given fasting on Day 1 and with a meal on Day 8.

HPN-100 was metabolized via the expected major pathway, from phenylbutyrate (PBA) to phenylacetic acid (PAA) and then to phenylacetylglutamine (PAGN). PAGN mediates waste nitrogen excretion and ammonia removal. The extent of plasma exposure to PAA significantly correlated with MELD score ($r^2= 0.15$; $p= 0.03$), but did not correlate significantly with glomerular filtration rate ($r^2= 0.01$; $p= 0.54$) or Child-Pugh score ($r^2= 0.10$; $p= 0.08$). No consistent differences between cirrhotic subjects and healthy volunteers were seen for the plasma PK variables on days 1 or 15. There were no statistically significant differences in the PK characteristics when HPN-100 was given fasting on day 1 or with a meal on day 8. Excretion of

the main metabolite PAGN was similar between healthy adults and cirrhotic subjects. Urinary PAGN after the first dose on Day 1 ranged from 42-49% of the administered dose, and the mean total excretion of PAGN after the last dose in the study (day 15) ranged from 25,152 to 31,431 umol in the four treatment groups

There were no SAEs or AEs leading to withdrawal during the study. The most common system organ class was "investigations" (32 events in 18 subjects), and of these the most frequent individual AEs were increased body temperature, which was reported in 10 subjects (all from Child-Pugh groups A, B, and C), and decreased platelet count, which was reported in 4 subjects in Child-Pugh group A and 1 subject in the healthy volunteer group. There were no overall consistent patterns across all subject groups in changes in mean hematology, biochemistry, and coagulation variables.

"Hepatic encephalopathy (HE) is a significant clinical problem," said Brendan M. McGuire, M.D. Medical Director of Liver Transplantation at the University of Alabama. "I am encouraged by the phase I study results and look forward to further clinical studies."

About HPN-100

HPN-100 is an investigational product that is a pre-pro-drug of phenylacetic acid, the active moiety of BUPHENYL(R), the only therapy currently FDA-approved as adjunctive therapy for the chronic management of patients with the most prevalent urea cycle disorders: carbamylphosphate synthetase (CPS), ornithine transcarbamylase (OTC) and argininosuccinic acid synthetase (AS) deficiencies. HPN-100, which is dosed orally in liquid form, is under clinical investigation as providing a potential alternative pathway to the urea cycle for the disposal of waste nitrogen through the renal excretion of phenylacetylglutamine (PAGN), which is formed from phenylacetic acid (PAA) and glutamine. Hyperion has initiated a phase III clinical program for the use of HPN-100 in the treatment of urea cycle disorders and plans to initiate a phase II program for the use of HPN-100 in treating hepatic encephalopathy later this year.

About Hepatic Encephalopathy

Hepatic encephalopathy (HE) is a serious but potentially reversible neurological disorder that can occur in patients with acute liver failure and, most commonly, in patients with cirrhosis of any etiology. It comprises a spectrum of neurological signs and symptoms ranging from mild (e.g. minimal disorientation) to severe (e.g. coma, death) and is believed to occur when the brain is exposed to gut-derived toxins such as ammonia that are normally removed from the blood by a healthy liver. There are no therapies currently FDA-approved for the treatment of HE.

About Urea Cycle Disorders

Urea cycle disorders are inherited, inborn errors of metabolism present in an estimated 1 in 10,000 births in the United States. Patients with urea cycle disorders are deficient in one of the key enzymes that comprise the urea cycle, the body's primary vehicle for removing ammonia, a potent neurotoxin, from the bloodstream. Onset may occur at any age depending on the severity of the disorder. Left untreated, urea cycle disorders can cause dangerously heightened levels of ammonia in the bloodstream (hyperammonemia) resulting in brain damage, coma, and/or death.

About BUPHENYL

BUPHENYL is indicated as adjunctive therapy in the chronic management of patients with urea

cycle disorders involving deficiencies of CPS, OTC, or AS. BUPHENYL should not be administered to patients with known hypersensitivity to sodium phenylbutyrate or any component of this preparation. The most common adverse reactions associated with BUPHENYL were amenorrhea dysfunction, decreased appetite, body odor (probably caused by its metabolite phenylacetate) and bad taste or taste aversion. Patients with urea cycle disorders should not take valproic acid, haloperidol, or steroids as these drugs have been reported to increase blood ammonia levels, and probenecid may affect the kidneys' excretion. Use with great care, if at all, in patients with congestive heart failure or severe renal insufficiency, and in clinical states where there is sodium retention with edema. Use caution when administering to patients with hepatic or renal insufficiency or inborn errors of beta oxidation. The safety or efficacy of doses in excess of 20 grams (40 tablets) per day has not been established.

About Hyperion Therapeutics

Hyperion Therapeutics is a privately held specialty pharmaceutical company focused on the development of therapies that address critical unmet needs in the areas of gastroenterology and hepatology. Hyperion and Ucyclid Pharma, Inc., a subsidiary of Medicis Pharmaceutical Corporation, entered into a collaboration agreement for HPN-100 in August 2007. Under the terms of the agreement, Hyperion is conducting ongoing research and development of HPN-100 for urea cycle disorders, hepatic encephalopathy, and other forms of hyperammonemia. Hyperion is headquartered in South San Francisco, CA.

BUPHENYL is a registered trademark of Ucyclid Pharma, Inc.

Source: Hyperion Therapeutics, Inc

"Make or break" time for health reform: Obama

www.reuters.com

Donna Smith

WASHINGTON (Reuters) - President Barack Obama stepped up efforts to build public support for a broad revamp of U.S. healthcare on Tuesday, saying the country could no longer afford the soaring costs of the current system that leaves millions without medical coverage.

"We cannot avoid bringing about change in our health care system," Obama told a group of Senate Democrats. "Soaring health care costs are unsustainable for families, they are unsustainable for businesses, and they are unsustainable for governments, both at the federal, state and local levels."

Obama's push on healthcare comes as lawmakers seek to craft a bill and pass it through the Senate before lawmakers take a summer break. Democratic leaders in the House of Representatives also hope to move health legislation through that chamber before August.

"This window between now and the August recess, I think, is going to be the make-or-break period," Obama said. "This is the time where we've got to get this done."

The White House Council of Economic Advisers issued a report on Tuesday saying that the overall U.S. economy would benefit significantly from an overhaul that reins in soaring costs and

expands medical coverage to an estimated 46 million uninsured.

Unsustainable Cost Increases

The White House report said healthcare spending, which currently accounts for about 18 percent of the country's economic output, could reach 34 percent by 2040 if the current rate of cost growth continues. The report called that outlook "unsustainable."

Most working Americans with health insurance get it through their employers and the study said rising costs have increased insurance premiums and cut into workers' wages. A reform that reins in costs would improve economic efficiency and boost economic output by more than 2 percent in 2020 and by 8 percent in 2030, the report concluded.

That would translate into \$2,600 in higher income for a family of four in 2020, rising to \$10,000 by 2030, the report said. Since about half of healthcare costs are paid by federal, state and local governments, their budgets also would benefit greatly by reform, it said.

Providing medical coverage to the uninsured will also help the economy by improving the overall well-being of the work force -- providing a net benefit to the economy of about \$100 billion a year, the report said.

Without the overhaul, the number of uninsured Americans would rise to about 72 million in 2040, it said.

Republicans were skeptical.

"This report is nothing more than smoke and mirrors. Everyone agrees that reducing the cost of health care would benefit our economy, but the administration hasn't offered a credible plan to do so without raising taxes or rationing care," House Republican Leader John Boehner said.

Covering the uninsured will be costly, just as U.S. government fiscal deficits are hitting record levels because of a huge economic stimulus package, financial and auto industry bailouts, and reduced revenue from taxes due to recession.

Lawmakers are trying to find cost savings through Medicare and Medicaid, the government health programs for the elderly and poor. The White House has proposed about \$300 billion in savings from those two programs.

Baucus also made clear he is considering limiting the tax benefits of employer-provided insurance.

Workers now pay no taxes on that benefit but Baucus said a cap on the tax exclusion would likely be a part of legislation his committee is writing, even though Obama opposes taxing employer-provided health benefits.

(Reporting by Donna Smith; Editing by Eric Walsh)

Belly fat tied to liver cancer recurrence

www.reuters.com

NEW YORK (Reuters Health) - The amount of fat accumulated around internal abdominal organs appears to affect the likelihood of a recurrence of liver cancer following treatment, Japanese researchers report.

Dr. H. Yoshida of the University of Tokyo and colleagues came to this conclusion after following 62 patients who had undergone treatment for liver cancer; 27 were classified as having high amounts of so-called "visceral" fat, while the other 35 had smaller amounts.

After a year, the recurrence rate was 15.9 percent in the high visceral fat group compared with 9.7 percent in the other patients.

After 3 years, the corresponding rates were 75.1 percent and 43.1 percent, the team reports in the issue of *Gut*.

During the observation period, there were 14 deaths, 9 of which were due to progression of liver cancer. However, there was no significant difference in survival between those with high amounts of belly fat and those with small amounts.

Meanwhile, the team concludes, "it remains to be seen" whether reducing levels of visceral fat decreases the odds of liver cancer returning.

SOURCE: Gut, June 2009.

ATC 2009: Patient and Graft Survival Near Equal in Matched HCV-Positive Liver Transplantation

<http://www.medscape.com>

Alice McCarthy

June 3, 2009 (Boston, Massachusetts) — A case-controlled, retrospective analysis of hepatitis C virus (HCV)-positive liver donations shows that recipient patient and graft survival are not affected by HCV-positive donor status when donor and recipient characteristics are matched.

The research was conducted on data gathered from the United Network for Organ Sharing (UNOS) database from 1987 to 2007 by investigators from the University of Massachusetts Medical School in Worcester.

"Diminished graft survival, risk of recurrent disease, and progressive fibrosis are all concerns with HCV-positive donated livers that may lead to inferior or marginal patient outcomes," Shimul Shah, MD, explained to attendees during his presentation here at the 2009 American Transplant Congress.

Numerous reports have documented reduced graft and patient survival after use of HCV-seropositive allografts in liver transplantation, according to the study abstract. Dr. Shah and

colleagues examined the UNOS database in a case-controlled analysis of donor and recipient characteristics to see if the use of a HCV-positive liver allograft affects patient and graft survival compared with HCV-negative donor allografts.

The investigators retrospectively examined 63,149 liver transplants (donor HCV-negative, n = 61,905; donor HCV-positive, n = 1244) from the UNOS Standard Transplant Analysis and Research (STAR) file.

Donor and recipient demographics and outcomes were collected for all transplantations in which donor HCV serology was complete. A case-controlled cohort from 9 important donor and recipient variables comparing donor HCV-negative and HCV-positive allografts (n = 1080) was created using a matching algorithm. Two matched groups of 540 cases each were identified with near-identical donor and patient characteristics. Approximately 80% of recipients in both matched groups were HCV-positive. Data on the 1080 cases was then reanalyzed to confirm that any differences between recipient and donor characteristics were eliminated. Primary endpoint, donor survival, and graft survival were estimated using Kaplan-Meier survival curves.

"In the unadjusted cohort, the patients who had the HCV-positive allograft had a diminished graft survival compared to HCV-negative donor allografts," said Dr. Shah. "Those patients also had worse survival." Specifically, use of HCV-positive allograft resulted in graft survival of 8.1 vs 10.6 years (P = .001), and patient survival of 10.2 vs 12.3 years (P = .01) for HCV-positive and HCV-negative donors, respectively.

"In this analysis, we found that there was no difference in graft and patient survival with use of HCV-positive allografts when controlling for donor and recipient characteristics," Dr. Shah said. "It was equal from the day of transplant out to about 1500 days.

"What we wanted to do was control for all the characteristics that are clinically important on the donor side and the recipient side to see if the outcomes truly are inferior," Dr. Shah told Medscape Transplantation. "And what we found is that they are not [inferior] when you control for all the important things, and we believe you can justify using these organs in patients who might not have HCV but who are critically ill or might need an emergency transplant.

"There is reluctance to use these allografts currently or they are only being used in HCV-positive recipients, as they probably should be primarily," Dr. Shah said. The investigators say these results suggest that HCV-positive donors remain an underused resource of potential donor allografts in liver transplantation.

"This analysis validates what most of us believe, that these livers can absolutely be used safely in patients that are already HCV-positive," Les Lilly, MD, director of transplant hepatology at the University of Toronto in Ontario, Canada, commented to Medscape Transplantation. "We all do this already but it is nice to see the results confirmed in such a large database."

Dr. Lilly, who was not involved in the study, agrees that the UNOS STAR file has many flaws, but it still represents the largest number of patients who have been looked at systematically. "But the data that are missing is important, too," he said. "It would be nice to know if you retrieve an organ from an HCV-positive patient if the patient still has the virus, since 25% of the people who get HCV get rid of the virus on their own. So maybe you aren't putting such rotten livers in as

you may think you are.

"This study justifies us doing what we're doing, and it's difficult to justify discarding any organ when we have such a huge gap between donors and those in need," Dr. Lilly said.

Dr. Shah and Dr. Lilly have disclosed no relevant financial relationships.

2009 American Transplant Congress (ATC): Abstract 51. Presented May 31, 2009.

Hepatitis B vaccine shortage: You may need to consider a different brand

<http://www.nephronline.com>

In December 2008, Merck told the Centers for Disease Control and Prevention that it expected to deplete available adult and dialysis formulations of their hepatitis B vaccine, Recombivax HB, in the first quarter of 2009. Once depleted, these formulations will be unavailable for the remainder of 2009.

According to the CDC, supply of Glaxo Smith Kline's adult hepatitis B vaccine (Adult Engerix-B) and adult hepatitis A/hepatitis B combination vaccine (Twinrix) is sufficient to meet demand for routine adult usage of this vaccine as well as CDC's ongoing High Risk Glaxo Smith Kline initiative.

This information is published at www.cdc.gov/vaccines/vac-gen/shortages/default.htm

Hepatitis B may increase all-cause mortality in HIV-positive people, according to meta-analysis

www.aidsmap.com

Kelly Safreed-Harmon

The first meta-analysis of all-cause mortality among people co-infected with hepatitis B and HIV has found this population to have a significantly higher rate of all-cause mortality than HIV-positive people without hepatitis B. The study is presented in the June 15th edition of *Clinical Infectious Diseases*, along with an editorial commentary calling for greater efforts to prevent and treat hepatitis B in co-infected individuals.

The study authors began their inquiry with a retrospective analysis of the impact of hepatitis B in a cohort of 1729 Greek adults diagnosed with HIV between 1984 and 2003. About 6% of study participants tested positive for hepatitis B on two occasions at least six months apart, suggesting chronic infection. Hepatitis B/HIV co-infection was not found to be significantly associated with any of the three primary outcomes of interest: progression to AIDS, antiretroviral efficacy, and all-cause mortality.

The authors next conducted a meta-analysis by combining their data with data from all relevant published studies. When data from 12,382 people enrolled in 11 studies were pooled, hepatitis

B/HIV co-infection was found to be significantly associated with all-cause mortality (pooled effect estimate, 1.36; 95% confidence interval [CI], 1.12–1.64).

Separate analyses for studies conducted before and after the advent of highly active antiretroviral therapy also yielded significant results. The pooled effect estimate for the earlier group of studies was 1.60 (95% CI, 1.07–2.39). The pooled effect estimate for the later group was 1.28 (95% CI, 1.03–1.60).

On the other hand, the pooled data provided no evidence of an association between hepatitis B/HIV co-infection and progression to AIDS.

Many of the studies in the meta-analysis took place in Western countries, and many enrolled men who have sex with men. The authors note that more research is needed among other populations before firmer conclusions can be drawn about the effect of hepatitis B/HIV co-infection on all-cause mortality.

One likely explanation for the higher rate of all-cause mortality in co-infected people is hepatitis B-related liver deterioration. Long-term hepatitis B infection can result in cirrhosis and liver cancer, both of which are potentially fatal.

However, the meta-analysis did not actually assess liver-related mortality, and it cannot be assumed that hepatitis B is the ultimate cause of the higher all-cause mortality rate. The editorial commentary accompanying the study observes that hepatitis B/HIV co-infection could be “a marker for other types of high-risk behavior that may place this population at an increased risk for death attributable to non-AIDS-related causes”.

In other words, the same behaviours that increase a person’s risk of acquiring hepatitis B, which is transmitted via bodily fluids, may also increase the person’s risk of developing other unrelated health problems that account for the higher all-cause mortality rate found in the meta-analysis.

Nonetheless, while the reasons for the higher mortality rate need to be further explored, what is already known about hepatitis B/HIV co-infection leads the author of the editorial review to make a series of recommendations. “Every HIV treatment provider must accurately diagnose hepatitis B infection, document the level of viremia prior to starting [antiretroviral therapy], and monitor hepatitis B ... levels to ensure that suppression is achieved,” the article says. It also advises providers to tell hepatitis B/HIV co-infected patients about the effect of alcohol consumption on the liver, and to screen for liver cancer.

When hepatitis B infection occurs, the immune system often clears hepatitis B from the body on its own. However, for people who do not experience viral clearance, treatment may be advisable. Treatment is only successful in about one-third of cases.

Hepatitis B virus treatment options are limited, and some treatment regimens have major drawbacks. Some antiretroviral drugs also work against hepatitis B, although hepatitis B resistance is likely to occur in response to 3TC (lamivudine, Epivir). Two other antiretrovirals with anti-hepatitis B activity are tenofovir (Viread) and FTC (emtricitabine, Emtriva).

If a co-infected person’s health status warrants simultaneous treatment for HIV and hepatitis B,

then an antiretroviral regimen that serves both purposes is recommended. However, when an HIV-positive person does not need antiretrovirals for management of HIV disease, using these drugs as hepatitis B treatment may be a questionable strategy given the risk of HIV resistance.

Because the risks and benefits of the various approaches to managing hepatitis B/HIV co-infection are not fully understood, more research is needed to inform treatment guidelines. The association between hepatitis B and all-cause mortality in the meta-analysis thus has important treatment implications. The accompanying editorial commentary states, “In light of the findings ... aggressive treatment of hepatitis B is warranted, including treating hepatitis B with ART regardless of CD4 cell count. Additional studies are needed to examine whether this strategy will lead to the desirable outcome of a decrease in the rate of death.”

Reference

Jain MK et al. Mortality in patients coinfecting with hepatitis B virus and HIV: could antiretroviral therapy make a difference? *Clinical Infectious Diseases* 48:(online edition) 2009.

Nikolopoulos GK Impact of hepatitis B virus infection on the progression of AIDS and mortality in HIV-infected individuals: a cohort study and meta-analysis. *Clinical Infectious Diseases* 48: (online edition) 2009.

June 4, 2009

Propylthiouracil May Increase Risk for Serious Liver Injury

<http://firstwatch.jwatch.org>

Adult and pediatric patients taking propylthiouracil (PTU) may be at increased risk for serious liver damage, including liver failure and death, the FDA announced on Wednesday. The drug is largely a second-line therapy for Graves hyperthyroidism.

The agency has tracked 32 cases of serious liver injury linked to PTU therapy. Thirteen patients died, and 11 required liver transplants.

The FDA advises clinicians to:

- use PTU only in patients who have an allergy or intolerance to methimazole, or in pregnant women in their first trimester;
- monitor patients on PTU for signs of liver damage, particularly during the first 6 months of therapy;
- have patients contact them if symptoms of liver injury occur, including fatigue, weakness, abdominal pain, itching, easy bruising, or yellowing of the eyes or skin;
- discontinue PTU use if liver damage is suspected.

[FDA alert](#)

Medical bills underlie 60 percent of U.S. bankrupts: study

www.reuters.com

Maggie Fox, Health and Science Editor

WASHINGTON (Reuters) - Medical bills are behind more than 60 percent of U.S. personal bankruptcies, U.S. researchers reported on Thursday in a report they said demonstrates that healthcare reform is on the wrong track.

More than 75 percent of these bankrupt families had health insurance but still were overwhelmed by their medical debts, the team at Harvard Law School, Harvard Medical School and Ohio University reported in the *American Journal of Medicine*.

"Unless you're Warren Buffett, your family is just one serious illness away from bankruptcy," Harvard's Dr. David Himmelstein, an advocate for a single-payer health insurance program for the United States, said in a statement.

"For middle-class Americans, health insurance offers little protection," he added.

The United States is embarking on an overhaul of its healthcare system, now a patchwork of public programs such as Medicare for the elderly and disabled and employer-sponsored health insurance that leaves 15 percent of the population with no coverage.

The researchers and some consumer advocates said the study showed the proposals under the most serious consideration are unlikely to help many Americans. They are pressing for a so-called single payer plan, in which one agency, usually the government, coordinates health coverage.

"Expanding private insurance and calling it health reform will fail to prevent financial catastrophe for hundreds of thousands of Americans every year," Dr. Sidney Wolfe of the Health Research Group at Public Citizen said in a statement.

About 170 million people get health insurance through an employer but President Barack Obama says soaring healthcare costs hurt the economy and force businesses to drop medical insurance for their workers.

Canceled Coverage

"Nationally, a quarter of firms cancel coverage immediately when an employee suffers a disabling illness; another quarter do so within a year," the report reads.

Obama told Congress on Wednesday he was open to making mandatory health insurance part of the overhaul.

Neither Congress nor Obama are considering the kind of single-payer plan advocated by Public Citizen, Himmelstein and his colleague Dr. Steffie Woolhandler.

"We need to rethink health reform," Woolhandler said. "Covering the uninsured isn't enough.

"Only single-payer national health insurance can make universal, comprehensive coverage affordable by saving the hundreds of billions we now waste on insurance overhead and bureaucracy."

The researchers studied 2,134 random families who filed for bankruptcy between January and

April in 2007, before the current recession began.

They used public bankruptcy court records and surveyed 1,032 people by telephone.

"Using a conservative definition, 62.1 percent of all bankruptcies in 2007 were medical; 92 percent of these medical debtors had medical debts over \$5,000, or 10 percent of pretax family income," the researchers wrote.

"Most medical debtors were well-educated, owned homes and had middle-class occupations."

The researchers, funded by the Robert Wood Johnson Foundation, said the share of bankruptcies that could be blamed on medical problems rose by 50 percent from 2001 to 2007.

Patients with multiple sclerosis paid a mean of \$34,167 out of pocket in 2007, diabetics paid \$26,971, and those with injuries paid \$25,096, the researchers found.

(Editing by Bill Trott and Jackie Frank)

Management of Incidental Hepatitis C Virus Infection — Polling Results

<http://content.nejm.org>

Marissa B. Wilck, M.D., Mary Beth Hamel, M.D., and Lindsey R. Baden, M.D.

In late April, we presented a case of a healthy black woman incidentally found to be infected with hepatitis C virus (HCV) in Clinical Decisions,¹ an interactive feature designed to assess how readers would manage a clinical problem for which there may be more than one appropriate approach to treatment. Our patient was a 25-year-old investment banker who had a positive result on an HCV antibody test when attempting to donate blood for the first time. She was in good health with no other known medical illnesses. She was seronegative for human immunodeficiency virus.

A total of 3216 votes were cast that could be attributed to a continent or region (Figure 1; also see the interactive map). Of the three treatment options proposed, the most popular — with 1400 votes (44% of the 3216 votes cast) — was the option to perform a liver biopsy and to base further treatment on the findings of the biopsy. The second most popular option, expectant management with periodic assessment of liver function, received 1086 votes (34% of the total), and the option to commence HCV therapy with peginterferon and ribavirin received 708 votes (22% of the total).

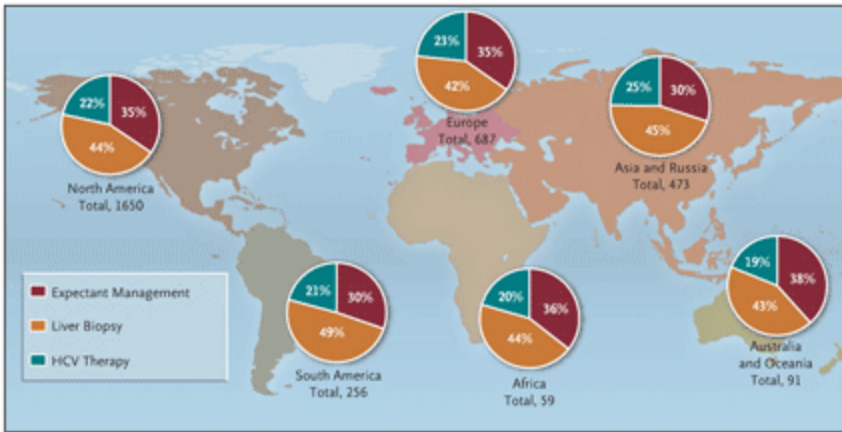


Figure 1. Percentage of Participants Choosing Each Option for the Management of Incidental Hepatitis C Virus Infection.

The total number of participants who voted and whose votes were attributable to a region and the percentage who chose each option are shown for each continent or region. Values may exceed 100% because of rounding. An interactive map that includes the total number of votes and percentages according to country is available at NEJM.org.

The 3216 voters were from 115 different countries and identified themselves as physicians (72%), medical students or physicians in training (16%), other health professionals (8%), or other (4%). The majority of the votes were from the United States (45%), followed by Italy (5%), the United Kingdom (4%), and Brazil (3%).

In addition to the votes, we received 201 comments from readers, of which 94% were posted at NEJM.org (after being reviewed for appropriateness). Some readers voiced the opinion that the patient should be presented with all three options and information regarding the risks and potential benefits for each and that the decision should then be based on the patient's wishes. However, the majority of the readers did go on to indicate which option they would choose. Many noted that some of the patient's laboratory values that appeared to be within the normal range (e.g., aspartate aminotransferase of 30 U per liter and platelet count of 175,000 per cubic milliliter) are most likely not normal for this woman and could indicate underlying liver disease. We also received a number of comments reflecting the struggle physicians and others have had with this disease and its treatment.

The majority of respondents who favored a liver biopsy to help guide further management highlighted the concern that liver-function tests do not serve as an accurate marker for liver damage² and that liver biopsy remains the standard test for staging liver disease. It was generally felt that that the liver biopsy would allow for the most informed management decision, justifying either the possible side effects of therapy or the delay of treatment until improved therapy became available, such as that described by McHutchison et al.³ and Hézode et al.⁴

The respondents favoring expectant management highlighted the patient's poor prognostic indicators for treatment success, such as infection with HCV genotype 1 and black race,^{5,6} and expressed concern that the side effects of therapy outweighed the low expected success rate of therapy. An overriding theme in support of this option was the hope that new and more potent

therapies would soon be available. Some suggested augmentation of the expectant management with noninvasive techniques to assess the degree of liver disease.

Conversely, others considered the patient's current good health to be a reason to choose the third option of immediate HCV therapy with peginterferon and ribavirin, arguing that she was in a position to tolerate the probable side effects of therapy and that the disease should be treated before it considerably damages her health. A number of readers voiced the concern of ongoing, possibly irreversible liver damage that could already be present and that could worsen while therapy is delayed. Some were concerned about the possibility that the patient would be lost to follow-up and that she might return for treatment only when she noticed clinically significant health effects — at which time much of the liver damage would be irreversible.

The votes and comments reflect the complexities related to the management of HCV infection and the difficulty of balancing commonly encountered treatment-limiting side effects and suboptimal response rates with the potential complications of untreated chronic infection.

From Brigham and Women's Hospital, Boston (M.B.W.).

No potential conflict of interest relevant to this article was reported.

References

1. Afdhal NH, Lok ASF, Di Bisceglie AM. Management of incidental hepatitis C virus infection. *N Engl J Med* 2009;360:1902-1906. [\[Free Full Text\]](#)
2. Pradat P, Alberti A, Poynard T, et al. Predictive value of ALT levels for histologic findings in chronic hepatitis C: a European collaborative study. *Hepatology* 2002;36:973-977. [\[ISI\]](#)[\[Medline\]](#)
3. McHutchison JG, Everson GT, Gordon SC, et al. Telaprevir with peginterferon and ribavirin for chronic HCV genotype 1 infection. *N Engl J Med* 2009;360:1827-1838. [\[Free Full Text\]](#)
4. Hézode C, Forestier N, Dusheiko G, et al. Telaprevir and peginterferon with or without ribavirin for chronic HCV infection. *N Engl J Med* 2009;360:1839-1850. [\[Free Full Text\]](#)
5. Fried MW, Shiffman ML, Reddy KR, et al. Peginterferon alfa-2a plus ribavirin for chronic hepatitis C virus infection. *N Engl J Med* 2002;347:975-982. [\[Free Full Text\]](#)
6. Conjeevaram HS, Fried MW, Jeffers LJ, et al. Peginterferon and ribavirin treatment in African American and Caucasian American patients with hepatitis C genotype 1. *Gastroenterology* 2006;131:470-477. [\[CrossRef\]](#)[\[ISI\]](#)[\[Medline\]](#)

J&J to seek approvals for slate of new drugs

www.reuters.com

NEW BRUNSWICK, N.J., June 4 (Reuters) - Johnson & Johnson (JNJ.N) told industry analysts on Thursday that it plans to seek approvals by 2010 for new drugs to treat hepatitis C and HIV, and to seek approvals by 2013 for at least eight other new treatments.

The diversified healthcare company said next year it will ask European regulators to approve Telaprevir, a high-profile pill for hepatitis C being developed in collaboration with Vertex

Pharmaceuticals Inc (VRTX.O). By next year it also plans to seek U.S. approval for HIV treatment TMC 278.

The company, reviewing its drug pipeline at a meeting in its hometown, said it plans to seek U.S. approvals between 2011 and 2013 for a so-called H3 antagonist for treatment of attention deficit hyperactivity disorder.

During that same time period, it said it also plans to seek U.S. approvals for a pain medicine that blocks a protein called NGF, a type 2 diabetes drug called Canagliflozin (SGLT-2), a so-called gut-specific MTP Inhibitor for obesity, a drug for multi-drug resistant tuberculosis called TMC-207, a treatment for hepatitis C called TMC 435 being developed in collaboration with Medivir AB (MVIRb.ST), its CNTO 328 treatment for a cancer called Castleman's disease and a rheumatoid arthritis drug called CNTO 136. (Reporting by Ransdell Pierson, editing by Gerald E. McCormick)

Anadys cuts jobs, program in restructuring move

<http://www.forbes.com>

SAN DIEGO -- Anadys Pharmaceuticals Inc. said Thursday it is cutting its work force by 40 percent, along with a drug development program, to focus resources on its lead hepatitis C drug candidate.

The restructuring move effects about 20 workers, while *the early-stage hepatitis C drug program for ANA773 will end. The focus will now be on ANA598*, which is heading into midstage development for hepatitis C.

The move comes as Anadys and other development stage biotechnology companies struggle with funding. Anadys had just \$4.7 million in cash and cash equivalents as of March 31, though that figure rises to \$20.8 million when marketable securities are included, the company has said.

Anadys said that figure would be sufficient to fund the company for 12 months, according to a Securities and Exchange Commission filing in April, but it would need additional funding to further develop its hepatitis C drug program. It now plans on raising about \$16.2 million through a stock and warrants offering to institutional investors.

ANA598 was given special "fast-track" review status by the Food and Drug Administration in 2008, allowing the company to submit its application in piecemeal fashion instead of all at once. Hepatitis C is a blood-borne infection causing liver inflammation and can eventually lead to liver failure or liver cancer. It affects about 3.2 million people in the U.S. and 170 million people worldwide.

The company expects a one-time charge of about \$1.3 million for severance costs and other costs associated with the restructuring move, but said it could save between \$4 million and \$5 million annually.

"As we complete preparations for the first Phase II study of ANA598 in combination with interferon and ribavirin, we have decided to focus our future investments on this important asset

and to take these cost-sparing measures which we expect to ensure our ability to complete the Phase II study with our expected cash resources," said Chief Executive Steve Worland, in a statement.

Anadys said the study could begin in the third quarter.

Shares of Anadys fell 8 cents, or 3.9 percent, to \$1.97 in morning trading, after losing as much as 11.7 percent earlier in the session. The stock has traded between \$1.50 and \$8.43 over the last 52 weeks.

Running in Tim's Name

<http://www.connectionnewspapers.com>

Bonnie Hobbs

Annual 5K fund-raising event is June 13.

There's still no cure for the hepatitis C that claimed Tim Harmon's life in 1999 at age 51. But it's hoped that funds raised by a 5K race in his honor will help toward that goal and also educate the public about this disease.

The 10th Annual Tim Harmon Memorial 5K Run/Walk is Saturday, June 13, at 8:30 a.m., rain or shine, at the Fairfax County Government Center. The course is mostly flat and fast, beginning and ending in front of the Government Center and going out to West Ox Road and Monument Drive.

Cost is \$21, and participants may register at www.racepacket.com, or in person on race day, from 7-8:15 a.m. For more information, call 703-934-8756, e-mail peggy.cook@fairfaxcounty.gov or see www.timharmon5k.org.

"Besides the runners, it attracts a mixture of people," said race director Tom Cook of Chantilly's Armfield Farms community. "A lot of them knew Tim and worked with him; others come to support friends and family members with hepatitis C. And they can either walk or run the course."

Harmon worked 20 years for Fairfax County and was director of Residential Services for Alcohol and Drug Services (ADS). He also founded a substance-abuse treatment program for teen-agers.

Because of his efforts, seven new residential treatment programs were opened. He also helped expand those at A New Beginning and Fairfax Detox in Chantilly, New Generations in Vienna, plus Crossroads and Sunrise House.

"Tim hired me in 1984 as a substance-abuse counselor [for ADS]," said Cook, who still holds that position and works with teens. "This county's lucky to have so many services, and Tim was a driving force behind a lot of them."

The race is held to remember Harmon and to raise awareness of hepatitis C. Proceeds go to

charities including the Hepatitis Foundation, the American Liver Foundation and local drug-treatment centers, including Sunrise in Fair Oaks.

Prizes in the 5K are awarded to the top three, male and female overall finishers, plus the top three finishers in 14 age groups in five-year increments. There are four race divisions: Runners/walkers, Fairfax County employees, baby joggers and public safety. Fire and police personnel will compete against each other for team and individual trophies.

Registered participants receive custom T-shirts designed by Kay Rankin. They're orange, black and white and feature an image of a runner. Said Cook: "I run in about 25 races a year, and it's always great to get a nice, bright T-shirt."

Sports Plus, Battlefield Screen, Cassaday Inc. and The Miller Firm are the major sponsors. And more than 100 trophies, plaques and medals will be presented, as well as door prizes from local restaurants and merchants.

They include Potomac Nationals baseball tickets, goody bags from Starbucks and gift certificates from Potomac River Running Store, Ledo's Pizza, Panera, Foster's Grille, Chipotle and J.R. Stockyards.

Silent auction items include signed footballs by Brian Griese of the Tampa Bay Buccaneers and his father Bob Griese, the Hall of Fame quarterback from the Miami Dolphins; a baseball signed by Washington Nationals outfielder Elijah Dukes; and gift certificates for rounds of golf at Osprey Bay Golf Course.

Adding to the fun is a live, classic-rock band, The Sock Monkeys, who'll entertain before, during and after the race. "They've played every year, since the first year, and are always a big hit," said Cook. And post-race refreshments such as bagels, granola bars, juice and soda will be available.

"Last year, we raised nearly \$13,000 and had 700 participants," said Cook. It costs about \$8,000 to put on the race, with the T-shirts and trophies being the biggest expenses. But Cook wouldn't dream of stopping.

"We start working on it in January and, after 10 years, it's what I do, each spring," he said. "Nine or 10 of us on the race committee have been on it for nine years. And we get a lot of positive feedback on the race — it's a great activity."

Literature in the race packets also helps educate people about hepatitis C and how to avoid contracting it. Harmon's disease was discovered through a routine blood test but, unfortunately, there's no vaccine for this silent killer.

And it has no symptoms, so people don't realize they have it until they're diagnosed. But by then, their livers may be irreparably damaged — and that's what happened to Harmon. For more information, call 1-800-891-0707 or see www.hepfi.org.

Harmon left behind a wife and two daughters, now grown. "Tim also has a 9-year-old grandson he never saw," said Cook. "Matthew was born the year after he died, and he comes to the race every year and participates."

NewYork-Presbyterian/Columbia physician-scientists present at 2009 American Transplant Congress

<http://www.eurekalert.org>

NEW YORK (June 4, 2009) -- NewYork-Presbyterian Hospital/Columbia University Medical Center physician-scientists presented new research at the 2009 American Transplant Congress in Boston, May 30 to June 3. Topics included minimizing steroid exposure for liver transplant patients with hepatitis C; hypothermic machine perfusion vs. cold storage for preserving donor livers; and the effectiveness of neutrophil-lymphocyte ratio in predicting colorectal liver metastases in liver cancer patients undergoing transplantation.

Dr. Jean Emond, chief of transplantation at NewYork-Presbyterian Hospital/Columbia University Medical Center and the Thomas S. Zimmer Professor of Surgery at Columbia University College of Physicians and Surgeons; and Dr. Robert S. Brown Jr., director of the Center for Liver Disease and Transplantation at NewYork-Presbyterian Hospital, chief of the Division of Abdominal Organ Transplantation and the Frank Cardile Professor of Medicine and Pediatrics in Surgery at Columbia University College of Physicians and Surgeons, are both available for comment on the following studies and on other news from the conference.

Preservation/Reperfusion Injury Is Attenuated by Hypothermic Machine Perfusion in Human Liver Transplantation.

Authors: Scot D. Henry, Ben Arrington, Benjamin Samstein, Sean W. C. Chen, Michael J. Goldstein, Jean C. Emond, H. Thomas Lee, James V. Guarrera

In hypothermic machine perfusion (HMP), a solution is pumped through the donor organ at temperatures between 1°C and 10°C in order to preserve the organ for transplantation. The technique is only just beginning to be used in liver transplantation. In a study comparing donor livers preserved using cold storage without perfusion to donor livers preserved with HMP, the latter were shown to be better preserved, with significantly improved functional and molecular markers.

Negative Impact of Neutrophil-Lymphocyte Ratio on Outcome Following Liver Transplantation for Hepatocellular Carcinoma (HCC).

Authors: Karim J. Halazun, Mark A. Hardy, Abbas A. Rana, David C. Woodland, Robert S. Brown, Jean C. Emond, Department of Organ Transplantation

A retrospective analysis looked at neutrophil-lymphocyte ratio (NLR) -- an indicator of inflammatory status previously established as a prognostic tool in colorectal liver metastases -- and found it to be an effective tool for predicting risk for tumor recurrence and death in liver cancer patients receiving transplantation.

Low-Dose Slowly-Tapered Steroids for Immunosuppression in Hepatitis C Virus Infected Liver Transplant Recipients: A 2-Year Follow-Up.

Authors: E. Verna, E. Pichardo, J. Emond, R. Brown Jr.

A two-year study of hepatitis C-infected patients receiving a liver transplant concluded that

reducing the dosage and slowing the taper of the steroid regimen did not affect outcomes. Reducing steroid exposure may lessen the side effects of high-dose steroids, including increased risk of cardiovascular disease, high cholesterol and blood pressure, weight gain, diabetes, bone weakness and cataracts.

The Effect of Socioeconomic Status on Survival and Fibrosis in Hepatitis C Virus Infected Liver Transplant Recipients: Experience at an Urban Referral Center.

Authors: Verna, E. Pichardo, E. Farrand, J. Emond, R. Brown Jr.

A retrospective study looked at the impact of socioeconomic status on the outcome of hepatitis C-infected patients receiving a liver transplant. They found that higher income is associated with improved one-year survival, but there was no association found between higher income and hepatitis C recurrence at one year.

Incisional Hernias and Liver Transplantation: Assessment of Clinical Practice and Outcomes.

Authors: B. Samstein, E. Pichardo, T. Perez, R. Brown Jr., J. Emond

Incisional hernias (IH) -- protrusion of an organ through the wall that normally contains it -- are a well-known complication following liver transplantation (LT). An analysis of patients receiving hernia repair found it to be safe and effective.

For more information, patients may call (866) NYP-NEWS.

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NEJM Study Points to New Era in Hepatitis C Treatment

<http://goodhealthstuff.org>

HCV Protease Inhibitor Telaprevir Improves Response, Halves Treatment Time for Hepatitis C Patients

For patients with the most common form of hepatitis C, the addition of a hepatitis C specific protease inhibitor called telaprevir to the current standard therapy can significantly improve the chances of being cured, and it does it in half the time of standard therapy alone.

Results of the Phase IIb clinical trial — led by Duke Clinical Research Institute (DCRI) and 36 other sites, including NewYork-Presbyterian Hospital/Weill Cornell Medical Center — are published in the April 30th issue of the *New England Journal of Medicine*. The study was funded by Vertex Pharmaceuticals Incorporated, the maker of the drug telaprevir. The drug works by blocking an enzyme that the hepatitis C virus needs in order to replicate itself.

“These findings point the way to a new era in the treatment of hepatitis C,” says Dr. Ira M. Jacobson, a co-author of the study and chief of the Division of Gastroenterology and Hepatology at NewYork-Presbyterian Hospital/Weill Cornell Medical Center, and the Vincent Astor Distinguished Professor of Clinical Medicine at Weill Cornell Medical College. “Not only does adding telaprevir make standard hepatitis C treatment more effective, but it makes it work much more quickly. We showed that the duration of therapy can be reduced from 48 weeks to 24

weeks for most patients. This could help reduce the potentially severe side effects of longer regimens with standard therapy.”

The randomized, double-blinded trial followed 250 patients with untreated hepatitis C genotype 1. Researchers measured rates of sustained viral response or viral cure — an undetectable quantity of hepatitis C virus — 24 weeks after the end of completion of therapy. They compared a 12-week regimen of telaprevir combined with two different durations of the standard therapy — peginterferon alfa-2a and ribavirin — to a control group taking 48 weeks of standard therapy alone. Results showed that 67 percent of patients taking telaprevir in combination with standard therapy for 12 weeks followed by standard therapy alone for 36 weeks were cured; and 61 percent of those taking telaprevir in combination with standard therapy for 12 weeks followed by standard therapy alone for 12 weeks were cured. This is compared to 41 percent cure rate in the 48-week control group.

The study also showed that the percentage of patients who relapsed in the 24-week and 48-week telaprevir-based groups (2 percent and 6 percent, respectively) was much lower than the control group (23 percent).

The most common reported side effect in the telaprevir groups was rash, and contributed to some patients discontinuing the therapy.

Peginterferon alfa-2a is an antiviral drug given by injection that is also used to treat HIV and hepatitis B; it works in conjunction with a drug called ribavirin, a nucleoside analogue, to suppress the viral activity of hepatitis C. Side effects can include severe flu-like symptoms, depression, fatigue, insomnia and anemia.

“Treating genotype 1 hepatitis C, the most common form of the infection in the United States, can be challenging because the side effects are difficult for many people to endure, the duration of treatment is long, and traditionally less than half of patients are able to be cured of their disease,” says Dr. Andrew Muir, a gastroenterologist at Duke Clinical Research Institute and a senior investigator on the study. “Even though telaprevir does produce side effects of its own, its addition to standard therapy was able to improve response rates and shorten the duration of treatment necessary — either one alone would have been an advance, and to be able to achieve both is a significant step in the right direction when it comes to treating hepatitis C.”

The study’s lead author is Dr. John McHutchison, a hepatologist and gastroenterologist and researcher at the Duke Clinical Research Institute. Additional co-authors include Drs. Gregory Everson of the University of Colorado Health Science Center; Stuart Gordon of Henry Ford Hospital; Mark Sulkowski of Johns Hopkins School of Medicine; and Robert Kauffman, Lindsay McNair and John Alam of Vertex Pharmaceuticals.

Drs. Jacobson, McHutchison and Muir have received consulting fees and/or grant support from Vertex, Roche (maker of peginterferon) and Schering-Plough (maker of ribavirin).

The study’s results match those of a similar study conducted in Europe that was reported on in the same issue of the *New England Journal of Medicine*. An accompanying editorial recounts the history of hepatitis C treatments, beginning 25 years ago with the discovery of interferon. It comments on the two studies: “Telaprevir appears to be a material advance in the therapy of

hepatitis C, beginning a new era of treatment — an era of antiviral agents developed specifically to target this virus.”

Two Phase III studies currently under way at New York-Presbyterian/Weill Cornell and centers worldwide will attempt to confirm the results, potentially leading to FDA approval of telaprevir. One study is looking at 12 weeks of telaprevir in combination with standard therapy (peginterferon alfa-2a and ribavirin) followed by either 12 or 36 weeks of standard therapy alone depending on patients’ response to therapy. A second study is comparing 8-week and 12-week regimens of telaprevir in combination with standard therapies followed by at least 12 weeks of standard therapy, depending on patients’ response to therapy, to a placebo group taking 48 weeks of standard therapy alone. Both studies are currently closed to recruitment.